#### REMARKS/ARGUMENTS

Pages 3 - 5 have been amended to provide sequence identification numbers as required by the Examiner on page 4 of the Office Action.

Paragraph 1 (in the Reference to Related Application) of the specification has been amended to claim the priority of the provisional application Serial No. 60/393,558, filed July 5, 2002.

Applicant respectfully requests reconsideration of the refusal to consider the Information Disclosure Statement filed on CD ROM in lieu of the paper copy. As cited in paragraph 5 of the Office Action, 37 C.F.R. 1.98(a)(2) only requires a legible copy, not a paper copy, and a CD ROM is a legible copy.

Claim 1 has been amended to recite computer mediated selective deletion and/or addition of connectrons to modify behavior of any genome.

Claims 1 and 2 are elected claims. Claims 3 - 12 have been withdrawn from consideration.

The rejection of claims 1 and 2 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, is respectfully traversed. The Examiner cites In re Wands, 8 USPQ2d 1400 (CFC 1988).

Claims 1 and 2 are short and read as follows:

1. (Currently Amended) The method of simulating connectron behavior of any genome for the purpose of modifying genomic

behavior comprising the <u>computer mediated</u> selective deletion and/or addition of connectrons.

2. (Original) The method of simulating connectron behavior of a genome for the purpose of modifying, by computer, genomic behavior comprising the selective deletion and/or addition of connectrons.

Note that the claims are specifically directed to methods of simulating connectron behavior by computer-mediated selective deletion and/or addition of connectrons.

Initially, it will be noted that this application is a continuation-in-part of application Serial No. 09/866,925 filed May 30, 2001, entitled "Algorithm determination of flanking DNA sequences that control the expression of sets of genes in prokaryotic, archea and eukaryotic genomes" which is on appeal from substantially the same ground of rejection. Applicant hereby incorporates by reference the points of argument made in an appeal brief as well as the declarations filed therein, a copy of which is attached.

Moreover, it will be noted that the present claims are directed to a method of <u>simulating</u> connectron behavior using computer mediated selective deletion and/or addition of connectrons. The Examiner contends that while the description provides guidance to identify connectron symmetries in genomic sequences: "The description does not provide detailed guidance to use identified connectron symmetries to predict an effect on gene expression." The claims only specify a

method of <u>simulating</u> connectron behavior of any gene "for the purpose of modifying genomic behavior" and not for the purpose of "providing detailed guidance to use identifying connectron symmetries <u>to predict</u> an effect on gene expression. Pages 15 and 16 of the specification set out specific objects of the invention as follows:

"An object of this invention is to provide a method for utilizing the genomic simulation of connectron behavior to facilitate the optimization of design decisions related to deleting connectrons from a genome or adding connectrons to a genome.

An object of this invention is to provide a method for utilizing the genomic simulation by computer of connectron behavior to facilitate the optimization by computer of design decisions related to deleting connectrons from a genome or adding connectrons to a genome.

An object of this invention is to provide a method for modifying the connectron behavior of a genome by deleting and adding connectrons.

An object of the invention is to provide a method for creating new connectrons in a genome by copying one or more double-stranded DNA sequence elements from one place in the genome to another place in the genome or by extracting a double-stranded DNA sequence element from one place in the genome and moving it to another place in the genome or by introducing a new unique pair of double-

stranded DNA sequence elements into the genome at specific places.

An object of the invention if to provide a method for creating new connectrons in a genome by copying, extracting or adding unique DNA elements in addition to using either DBPs, PNAs or a linked pair of generalized DNA binding elements to implement the C1 and C2 elements of the new connectron."

None of these objects seeks to "predict regulation of gene expression." As stated by Mr. Oberthaler, the algorithms presented are straightforward and complete:

"No experimentation whatsoever is required. Implementing the algorithms is a routine exercise in program design, coding and debugging. Running them is simply a matter of obtaining the organism-specific genomes and allowing the computer programs to go to work on them.

The only part of the activity that could conceivably be referred to as "experimenting" is the investigation into available bioinformatics resources, such as the syntax and semantics of the resources provided by, for example, that National Library of Medicine's National Center for Biotechnology Information (NCBI). It is clear that in this context, having a ready understanding of this information

is a reasonable characteristic of one who could be called "skilled in the art.""

Hence, no undue experimentation is required in order to practice the invention.

In view of the above, further and favorable reconsideration is respectfully requested.

Further to the Examiner's requirement, a new Sequence Listing Disc and paper copy of the Sequence Listing are attached. The content of the sequence listing information recorded in computer readable form is identical to the written sequence listing (paper copy attached) and includes no new matter.

Respectfully submitted,

Jim Zegeer, Reg. No. 18,957 Attorney for Applicant

Attachments: Copy of Brief filed in Serial No. 09/866,925

Sequence Listing Disc and Paper Copy

of Sequence Listing

Suite 108 801 North Pitt Street Alexandria, VA 22314 Telephone: 703-684-8333

September 22, 2006 Date:

In the event this paper is deemed not timely filed, the applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to Deposit Account No. 26-0090 along with any other additional fees which may be required with respect to this paper.

Atty. Docket No.: 3124-Z

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Richard J. Feldmann

Serial No. 09/866,925 Filed: May 30, 2001 Group Art Unit 1645

Examiner John S. Brusca

For: Algorithmic determination of flanking DNA sequences that control the expression of sets of genes in

prokaryotic, archea and eukaryotic genomes



## AMENDED BRIEF ON APPEAL

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

This is an appeal from the final rejection mailed September 23, 2004 of Claims 20 - 37 of the above-identified application.

# (i). The Real Party in Interest

The real party in interest is Global Determinants, Inc.

# (ii). Related Appeals and Interferences

There are no related appeals or interferences.

# (iii). Status of the Claims

Claims 20 - 37 are pending in the application and have been finally rejected and are all on appeal. Claims 1 - 19 have been cancelled.

## (iv). Status of the Amendments

There was no amendment filed subsequent to the final rejection.

## (v). Summary of Claimed Subject Matter

The invention is directed to a computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome. DNA sequences of an organism (the genome thereof) are analyzed by computer to identify DNA control sequences, called C1, C2 in the algorithm which meets certain specific criteria set forth at pages 26-36 of the description. Further, identified sequences behave in such a way that when the control sequence (C1 and C2) is transcribed into RNA, the RNA will seek out and bind the target sequences T1 and T2 (C1 binding to T1 and C2 binding to T2) to achieve the effect that the entire DNA sequence beginning with T1 and ending with T2 is shielded from transcription.

# (vi). Grounds of Rejection to be Reviewed on Appeal

The final rejection of claims 20 - 37 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and/or use the invention?

## (vii). Argument

The claims stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, the Examiner citing *In re Wands*, 8 USPQ2d 1400 (CAFC 1988).

The claims are all directed to computer mediated methods of genome investigation in which the tetradic relationship between two specific adjacent RNA single-stranded sequences interact with two different double-stranded DNA sequences. Claim 20 refers to a computer algorithm for identifying DNA sequences that control the expression of different collections of genes of a genome comprising detecting by computer one or more pairs of non-adjacent DNA sequences in which are bound one RNA molecule comprising two RNA sequences. In re Wands does not deal with computer mediated matters.

In rebuttal to the 35 U.S.C. §112, first paragraph, rejections, appellant submitted two declarations, one of Dr. Richard W. Pastor, and the second of James B. Oberthaler.

Both declarations traverse the Examiner's conclusion that undue experimentation is necessary in order to practice the invention. The Oberthaler<sup>1</sup> declaration concludes:

Mr. Oberthaler has a minority interest (less than 10%)
in a licensee of the invention.

Finally, in conclusion, I disagree with the Examiner's contention that the trial and experimentation required to practice the invention amounts to undue experimentation for the following reasons:

- (1) As stated earlier, the algorithms presented are straightforward and complete.
- (2) No experimentation whatsoever is required. Implementing the algorithms is a routine exercise in program design, coding and debugging. Running them is simply a matter of obtaining the organism-specific genomes and allowing the computer programs to go to work on them.
- (3) The only part of the activity that could conceivably be referred to as "experimenting" is the investigation into available bioinformatics resources, such as the syntax and semantics of the resources provided by, for example, that National Library of Medicine's National Center for Biotechnology Information (NCBI). It is clear that in this context, having a ready understanding of this information is a reasonable characteristic of one who could be called "skilled in the art."

(Note: Even In re Wands recognized that some experimentation is permissible. 84 USPQ 1400, at p. 1404.)

## Dr. Pastor states as follows:

The skilled practitioner would turn to the instant description and drawings for guidance in using the claimed invention. The specification provides a detailed roadmap for practicing the invention by one skilled in the art. Referring specifically to the specification and drawings, the introduction at pages 1 - 3 provides a basic description of connectron structure. Figures 1 -3 are taken from the text by Alberts et al. entitled "The Molecular Biology of the Cell." Pages 3 - 25. Pages 26 - 36 provides a detailed description of a connectron structure. Page 31, the detailed description of the invention, provides a descriptive analysis of the flow diagrams utilized in the computer analysis of connectrons Additionally, ten samples of in any given genome. connectrons found by computer mediation are set out in the specification. Pages 39 - 56 give an example of a prokaryote connectron - E. coli. hence, the algorithm is clearly defined and could be programmed by a skilled scientist. In this sense, the amount of experimentation is quite predictable.

I agree that the nature of the invention, gene control, is complex, and that prior art does not discuss connectron symmetries; i.e., it is my understanding and belief that the connectron invention disclosed in the instant application was made by the inventor, Richard J. [The page references are to the original specification.]

To the extent that In re Wands applies to claims dealing with computer mediated genome matters, the Oberthaler and Pastor that undue Examiner's contention declarations the rebut experimentation is necessary in order to practice the invention. Both declarations clearly establish that a detailed roadmap for practicing the invention by one skilled in the art is given in the Both declarations traverse the Examiner's conspecification. clusion that undue experimentation is necessary in order to practice computer mediating steps recited in the claims. Oberthaler declaration establishes that one skilled in the art (a journeyman, molecular biologist, bioinformatician, or computer programmer who understands the storage format, content and use of readily available bioinformatics resources) can write software following the algorithm that will analyze the DNA sequence of an organism to identify DNA sequences (called C1, C2, T1, T2 in the description of the algorithm) meeting specific criteria set forth in the description. And, further, that the identified sequences behave in such a way that when the control sequence containing C1 and C2 is transcribed into RNA, the RNA will seek out and bind to the target sequence (C1 binding to T1 and T1 and C2 binding to T2 to achieve the effect that the entire DNA sequence beginning with T1 and ending with T2 is shielded from transcription. (See page 4 of the Oberthaler declaration.)

In support of his contention, the Examiner refers to page 29, paragraph 113 of appellant's specification that: "The physical existence and lifetimes of the connectrons must be proved by molecular biological experimentation." This, however, is taken out of context. The full paragraph reads as follows:

The physical existence and lifetimes of the connectrons must be proved by molecular biological experimentation. This physical experimentation process, however, is logically quite separate from the computational experimentation that have been conducted from June of 1999 to May of 2001. The computational search for the existence of connectrons has been extremely positive. These computations have shown that connectrons exist in prokaryotes, in archea, between prokaryotes and their plasmids, in single-celled eukaryotes, in multi-celled eukaryotes, in plants, in higher animals and in humans. All of these features and properties are described in the claims section that follows.

The physical experimentation process is quite separate from the computational experimentation that has been conducted. Appellant respectfully submits that these declarations fully refute the Examiner's contention that claims 20 - 37 contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make or use the invention and that undue experimentation is required.

With respect to the Examiner's contention that the description does not provide working examples of using identified connectron symmetry to predict effects on gene expression (page 3 of Office action), item subparagraph c)), Mr. Oberthaler states:

I disagree. On the contrary, this is exactly what the examples provide. As explained in the introduction and in the definitions provided, (particularly, the definitions of Possible Connectron and Hierarchy of Connectron Action) each connectron control sequence C1-C2 will, when transcribed into RNA, seek out and bind to its target sequence T1-T2, thereby shielding the DNA between T1 and T2 from transcription. Since the shielded DNA sequence will not be transcribed, any genes in the span between T1 and T2 will not be expressed as proteins for as long as the C1-C2 sequence remains bound to T1-T2. Similarly, any additional C1-C2 sequences in the span between T1 and T2 will also remain inactive during this time period, and therefore the inability effect they otherwise would have exerted on their target sequences will be suppressed during this time period. Granted that the full, cascading sequence of transcription/expression and sequestration that would result from each of the examples discussed is not presented, the principles are given that would enable anyone who understands the mechanism, as explained in the application, to follow the effects as deeply as he or she desires.

Claim 21 is directed to a computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising, by computer, detecting changes in connectron behavior in a genome as a function of changes in the sequence of the genome.

Claim 22 differs in that this claim is directed to a computer mediated method of detecting changes caused by the application of an exogenous stimulus.

Claim 23 differs in that this claim is directed to a method of detecting by computer where and when new genes have been integrated into a host genome comprising detecting an operable link between a newly introduced gene and a preexisting connectron behavior in the host genome.

Claim 24 is directed to a computer mediated method of detecting the expression effect of different gene collections comprising detecting by computer the effect of connectrons on transcription.

Claim 25 is directed to a method of changing the expression of different gene collections in a genome by identification of connectron organization.

Claim 26 is directed to a method of detecting connectron control and target sequences in a given genome by computer, determining the base composition of the genome, determining one or more sites of control sequence organization, and/or determining one or more sites of target application.

Claim 27 is directed to a computer mediated method of determining the response of a cell in any tissue to changes in the cell's environment and/or genetic composition, by computer, providing a complete genomic DNA sequence for the organism and determining the effect of changes in connectrons due to application of a given exogenous stimulus to the genome.

Claims 28 - 37 are dependent from claim 20 and stand or fall with that claim.

resources available to corporations and research institutions.

Appellant respectfully submits that the Examiner erred in finally rejecting claims 20 - 37 and should be reversed.

Respectfully submitted,

Attorney for Appellant

Jim Zegeer, Reg. No. 18,957

Attachment: CLAIMS APPENDIX EVIDENCE APPENDIX

Suite 108 801 North Pitt Street Alexandria, VA 22314 Telephone: 703-684-8333

Date: August 5, 2005

In the event this paper is deemed not timely filed, the applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to Deposit Account No. 26-0090 along with any other additional fees which may be required with respect to this paper.

## (viii) CLAIMS APPENDIX

20. A computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising detecting, by computer, one or more pairs of first and second non-adjacent DNA sequences which could bind to one RNA molecule such that a first RNA sequence in that RNA molecule can bind to a first non-adjacent DNA sequence and a second RNA sequence in that RNA molecule can bind to a second non-adjacent DNA sequence.

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- 21. A computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising, by computer, detecting, by computer, changes in connectron behavior in the genome as a function of changes in the sequence of the genome.
- 22. A computer mediated method of detecting changes in expression of different gene collections in a genome, comprising: by computer, detecting changes in expression of different gene collections in a genome that result in changes in the level of connectron control sequences caused by an exogenous stimulus.
- 23. A computer mediated method of detecting, by computer, where and when new genes have been integrated into a host genome comprising detecting an operable link between a newly introduced gene and a preexisting connectron behavior in said host genome.
- 24. A computer mediated method of detecting the expression effect of different gene collections in a given host genome, comprising: by computer, detecting the effect of connectrons on transcription.

- 25. A computer mediated method of changing the expression of different gene collections in a genome comprising modifying, by a computer, identification of connectron organization.
- 26. A method of detecting connectron control and target sequences in a given genome comprising:

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by computer, determining the base composition of said genome, determining one or more sites of control sequence organization, and/or determining one or more sites of target application.

- 27. A computer mediated method of determining the response of a cell in any tissue to changes in the cell's environment and/or genetic composition comprising: by computer, providing a complete genomic DNA sequence for the organism and determining the effect of changes in connectrons due to application of a given exogenous stimulus to the genome.
- 28. Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequence and the RNA molecule can form a tetradic relationship such that T1=C1 and T2=C2 where T1 and T2 are DNA sequences 20 or more bases in length, where the C1 sequence is adjacent to the C2 sequence, where the T1 and T2 sequences are on the same chromosome, and where the C1/C2 sequences are on the same chromosome as T1 and T2 or where the C1/C2 sequences are on a chromosome different from T1 and T2, wherein:
- C1 sequence any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

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C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

- 29. Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a connectron that permits many different C1/C2 short loops to control the existence of a T1-T2 long loop and wherein said C1/C2 short lops can be on the same chromosome or on different chromosomes from the T1-T2 long loop, wherein:
  - C1 sequence any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,
  - C2 sequence any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

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T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

30. Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a connectron that permits one C1/C2 short loop to control the existence of many T1-T2 long loops, the C1/C2 short loop can be on the same chromosome or on different chromosomes from the T1-T2 long loops, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

 ${\rm C1/C2}$  - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

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T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

- 31. Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a connectron between prokaryotes and their plasmids and wherein said connectron implements a control mechanism between the two genomes that makes it possible from them to form a symbiotic relationship, and in the case of D. radiodurans the relationship is not symmetric, and the D. radiodurans genome sends C1/C2 short loops to the MP1 plasmid, wherein:
- C1 sequence any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,
  - C2 sequence any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,
  - C1/C2 any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,
  - T1 sequence any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2

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sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

- 32. Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a connectron that exist in a plant or a higher animal.
- 33. Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a connectron that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops without being subject to any expression controls other than those of the gene to which the C1/C2 is 3'UTR, wherein:
  - C1 sequence any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,
  - C2 sequence any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,
  - C1/C2 any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,
  - T1 sequence any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2

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T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart, and

3'UTR - untranslated 3' end of an mRNA is beyond the end of the last exon, a stop codon in the mRNA causes the ribosome to stop the translation of mRNA into protein.

- 34. Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a connectron that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops such that this C1/C2 short loop is itself subject to expression control by another T1-T2 long loop which surrounds it, wherein:
  - C1 sequence any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,
  - C2 sequence any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,
  - ${\rm C1/C2}$  any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,
  - T1 sequence any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

35. Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a connectron that permits one C1/C2 short loop to control the existence of the T1-T2 long loop that surrounds it, wherein:

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C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

 ${\rm C1/C2}$  - any positive or negative strand DNA sequence of 50 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1

sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

36. Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a connectron that does not have any genes within the T1-T2 long loop, wherein:

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T1 sequence is any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, and the T2 or T1 sequences must be between about 1kb and 105kb apart.

37. Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a geneless connectron where one C1/C2 short loop controls the existence of many geneless T1-T2 long loops, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

 ${\rm C1/C2}$  - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

# (ix). EVIDENCE APPENDIX

- 1. Declaration Under 37 C.F.R. §1.132 (Richard W. Pastor)
- 2. Declaration Under 37 C.F.R. §1.132 (James V. Oberthaler)

The above two Declarations were filed in the USPTO with applicant's response on June 9, 2003.

See the Examiner's rejection in the Office Action mailed October 8, 2003 at page 4, paragraph 10.

# (x). RELATED PROCEEDINGS APPENDIX

There are no proceedings as mentioned in section (i) above, and accordingly no decisions rendered.